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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/009,846	01/20/98	ZAMBIAS	R 5925-061-999

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HM12/0425

EXAMINER

PONNALURI, P

ART UNIT	PAPER NUMBER
1627	31

DATE MAILED: 04/25/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

Application No.

09/009,846

Applicant(s)

Zambias et al

Examiner

P. Ponnaluri

Art Unit

1627

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on Feb 7, 2001.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 10-13, 17, 18, and 20-25 is/are pending in the application.
- 4a) Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 10-13, 17, 18, and 20-25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some\* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

- 15) ☐ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 18) ☒ Interview Summary (PTO-413) Paper No(s) 30
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other:

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### **DETAILED ACTION**

1. The amendment filed on 2/7/01 has been fully considered and entered into the application.
2. Claims 10-13, 17-18 and 20-25 are currently pending and are being examined in this application.
3. The rejections of claims 10, 11, 12 and 22 under 35 U.S.C. 112, second paragraph rejection set forth in the previous office action paragraph has been withdrawn in view of applicants arguments.
4. The rejection of claims 20, 21, and 25 under 35 U.S.C, 112, second paragraph, is maintained for the reasons set forth in the previous office action.
5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
6. Claims 10-13, 17-18 and 20-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over combined teachings of Pirrung et al (Advance ACS Abstract, vol. 8, No. 1, January 1, 1995) and Gallop et al (Journal of Medicinal Chemistry, vol. 37, number 9, April 29, 1994, pages 1233-1251) for the reason set forth in the previous office action.

#### ***New Grounds of rejections necessitated by the amendments***

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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8. Claims 20, 21 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claims 20, 21 and 25 recite 'further comprising the step of screening the compounds...'. Claim is incomplete and omits essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the claims do not recite how the compounds of the array or subarray are screened. And the claim do not recite for what the compounds are screened for. Is the screening is performed to identify a compound with biological activity or for a specific structural property? The claims do not recite how the compounds are screened. Does the method uses analytical methods (such as NMR, Mass spectrometer) or biological methods. Thus, the claims are incomplete. Applicants are requested to amend the claims.

#### ***Response to Arguments***

10. *Applicant's arguments filed on 2/7/01, regarding the rejection of claims 20, 21 and 25 under 35 U.S.C. 112, second paragraph, of record have been fully considered but they are not persuasive.*

*Applicants argue that the screening of compounds for 'structure activity relationship' is well known, and one of ordinary skill in the art would be able to perform the claimed methods using no more than routine experimentation. Applicants arguments have been considered but are not persuasive, because the compounds of the library are supposed to be novel, and it is not*

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*clear for what property the compounds are screened, and how they are screened. Without the specific teachings for which property the compounds are screened or the how they are screened (is it using analytical methods such mass spectrometry or NMR, or biological assays), the claim is incomplete.*

11. *Applicant's arguments filed on 2/7/01, regarding the art rejection of record have been fully considered but they are not persuasive.*

*Applicants argue that the Pirrung neither teaches nor discloses methods for the generation of solution phase libraries as presently claimed, and Pirrung provides no experimental details about the structures of the compounds, nor about the specific methods by which the compounds are made. Applicants arguments have been considered but are not persuasive. Because the reference do not explicitly teach that the compounds are made by solution phase, however, the reference teaches that the compounds are 'free form', which means that the compounds are not attached to solid supports. That would mean that the compounds are in solution phase. Applicants arguments regarding that the reference did not provide details of the structures of the compounds are not persuasive. Because the reference teaches that the 'the reacting compounds is fixed and the other reactants were used in equimolar mixtures.' And the reference teaches that nine alcohols and six isocyanates (refers first and second reactants of the instant claims) are reacted to form carbomates. The reference teaches to deduce most active member of the library, it was prepared as 15 sublibraries (refers to sub arrays of the instant*

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*claims). The reference also teaches that the Indexed libraries offer the advantage that they can be prepared from any class of compounds composed of multiple subunits.*

*Applicants argue that Pirrung et al does not teach or suggest the synthesis of at least 500 different compounds in solution phase. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). This rejection is based on combined teachings of Pirrung et al and Gallop et al . Pirrung et al do not teach 500 different compounds in the library. However, Gallop et al teach that depending on the number of individual compounds in a library (N) depends on the number of building blocks (b) (reactants) available for each step, and the number of reaction steps in reaction scheme (x), and  $N = b^x$ . i.e., the reference teaches that using 100 building blocks permits the theoretical synthesis of 100 million tetrameric chemical entities. Thus, one skilled in the art at the time the invention was made would know to make 500 different compound array using the teachings of Gallop et al*

*In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine, 837 F.2d 1071,*

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5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the Gallop et al reference (a review article) teaches that the chemical libraries are intentionally created collections of differing molecules which can be prepared either synthetically or biosynthetically and screened for biological activity in a variety of different formats (e.g., libraries of soluble molecules....). Thus the reference teaches that the combinatorial libraries can be made in solution phase. The reference in page 1234, (left column, first two paragraphs) teaches the use of building block approach to create 'chemical libraries', and teaches the reaction scheme. The reference during the discussion nowhere discusses that the building block approach is not useful in solution phase or it is useful only with solid phase synthesis. Thus, it would have been obvious to a person skilled in the art at the time the invention was made to combine the building block approach of Pirrung et al with the 'Indexed library' method taught by Pirrung et al to make an array of 500 different compounds. Applicants argue that the 'split synthesis' method taught by Gallop et al is solid phase synthesis which can not be combined with solution phase synthesis of Pirrung et al. Applicants arguments are not persuasive, because the 'split synthesis method' discussed by Gallop et al is a general method, even though Gallop et al teach in reference to solid phase synthesis. The split synthesis method could be used for solution phase synthesis. The instant claimed method recites the reactions in test tubes, it is not clear how it would be different from the solid phase synthesis in which the reactants are attached to substrates and placed in vessels or tubes. Each test tube in the instant method could be equal to solid support of the split method. Applicants argue that the solid phase

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*methods described by Gallop et al are not applicable to the solution phase methods of the instant methods. Applicants arguments are not persuasive. Applicants have not pointed out how the instant method compounds would be different from the reference (by not using the solid supports) during the synthesis, since the instant method compounds (reactants) are in the test tubes which would be equal to the compounds (reactants) attached to beads and placed in vessels taught by the reference. The compounds are in solution phase or attached to the solid supports would only make a difference during testing or screening. Since the solid phase bound compounds may not interact with the testing compound as freely as the solution phase or free form compounds. However, Pirrung et al teach solution phase method in synthesis of combinatorial library of compounds. Pirrung et al teach the advantages of the free form of compounds in a library. Gallop et al teach the solution phase method of combinatorial library. Gallop et al teach solid phase split pool synthesis method in synthesis of combinatorial library. Since Pirrung et al teach the advantages of the solution phase synthesis and Gallop et al teach solution phase synthesis, it would be obvious to one skilled in the art to combine the teachings of split pool synthesis method taught by Gallop et al with the solution phase synthesis taught by Pirrung et al The rejections have been maintained for the reasons of record.*

12. No claims are allowed.
13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).



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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication should be directed to P. Ponnaluri whose telephone number is (703) 305-3884. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat, can be reached at (703)308-2439. The fax number for this group is (703)305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the group receptionist whose telephone number is (703)308-0196.



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Art Unit 1627  
20 April 2001